Practitioner's Docket No. MPI00-252P1RM

IN THE SPECIFICATION

At page 3, line 13 through page 4 line 6, please replace the paragraph with the following text:

Accordingly, in one aspect, the invention features a nucleic acid molecule that encodes a 52906, 33408, or 12189 protein or polypeptide, e.g., a biologically active portion of the 52906, 33408, or 12189 protein. In a preferred embodiment the isolated nucleic acid molecule encodes a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:8. In other embodiments, the invention provides isolated 52906, 33408, or 12189 nucleic acid molecules having the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7~~, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~. In still other embodiments, the invention provides nucleic acid molecules that are substantially identical (e.g., naturally occurring allelic variants) to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7~~, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~. In other embodiments, the invention provides a nucleic acid molecule which hybridizes under a stringency condition described herein to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7~~, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ____~~, wherein the nucleic acid encodes a full length 52906, 33408, or 12189 protein or an active fragment thereof.

At page 4, line 27 through page 5 line 16, please replace the paragraph with the following text:

In other embodiments, the invention provides 52906, 33408, or 12189 polypeptides, e.g., a 52906, 33408, or 12189 polypeptide having the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:8~~, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ____, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ____, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ____~~; an amino acid sequence that is substantially identical to the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:8~~, the amino~~

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~~acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ___, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ___, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ___~~; or an amino acid sequence encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under a stringency condition described herein to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, ~~the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ___, the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ___, or the sequence of the DNA insert of the plasmid deposited with ATCC Accession Number ___~~, wherein the nucleic acid encodes a full length 52906, 33408, or 12189 protein or an active fragment thereof.

At page 11, line 25 through page 12 line 3, please replace the paragraphs with the following text:

For general information regarding PFAM identifiers, PS prefix and PF prefix domain identification numbers, refer to Sonnhammer *et al.* (1997) *Protein* 28:405-420 and ~~http://~~www.psc.edu/general/ software/packages/pfam/pfam.html.

~~A plasmid containing the nucleotide sequence encoding human 52906 (clone "Fbh52906FL") was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on ____ and assigned Accession Number ____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

At page 13, lines 24-30, please replace the paragraph with the following text:

~~A plasmid containing the nucleotide sequence encoding human 33408 (clone "Fbh33408FL") was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on ____ and assigned Accession Number ____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

At page 15, lines 11-17, please replace paragraph with the following text:

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~~A plasmid containing the nucleotide sequence encoding human 12189 (clone "Fbh12189 FL") was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on _____ and assigned Accession Number _____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

At page 15, line 22, please replace the table with the following text, removing the entire fifth column:

Table 1: Summary of Sequence Information for 52906, 33408, and 12189

Gene	cDNA	ORF	Polypeptide	~~ATCC Accession Number~~
52906	SEQ ID NO:1	SEQ ID NO:3	SEQ ID NO:2	~~_____~~
33408	SEQ ID NO:4	SEQ ID NO:6	SEQ ID NO:5	~~_____~~
12189	SEQ ID NO:7		SEQ ID NO:8	~~_____~~

At page 21, lines 14-30, please replace the paragraph with the following text:

As used herein, the term "ion transport protein domain" includes an amino acid sequence of about 100 to 300 amino acid residues in length and having a bit score for the alignment of the sequence to the ion transport protein domain profile (Pfam HMM) of at least 50. Preferably, a ion transport protein domain includes at least about 150 to 280 amino acids, more preferably about 170 to 260 amino acid residues, or about 180 to 230 amino acids and has a bit score for the alignment of the sequence to the ion transport protein domain (HMM) of at least 90 or greater. The ion transport protein domain (HMM) has been assigned the PFAM Accession Number PF00520 (~~http://~~genome.wustl.edu/Pfam/.html). An alignment of the ion transport protein domain (amino acids 472-661 of SEQ ID NO:2) of human 52906 with a consensus amino acid sequence (SEQ ID NO:9) derived from a hidden Markov model is depicted in Figure 2. An alignment of the ion transport protein domain (amino acids 247-467 of SEQ ID NO:5) of human 33408 with a consensus amino acid sequence (SEQ ID NO:9) derived from a hidden Markov model is depicted in Figure 4A. An alignment of the ion transport protein domain (amino acids 198-383 of SEQ ID NO:8) of human 12189 with a consensus amino acid sequence (SEQ ID NO:9) derived from a hidden Markov model is depicted in Figure 6B.

At page 22, lines 10-22, please replace the paragraph with the following text:

As used herein, the term "cyclic nucleotide binding domain" includes an amino acid sequence of about 40-180 amino acid residues in length and having a bit score for the alignment of the sequence to the cyclic nucleotide binding domain (HMM) of at least 50. Preferably, a cyclic nucleotide binding domain is capable of binding a cyclic nucleotide. Preferably, a cyclic nucleotide binding domain includes at least about 50-150 amino acids, more preferably about 70-120 amino acid residues, or about 80-100 amino acids and has a bit score for the alignment of the sequence to the cyclic nucleotide binding domain (HMM) of at least 80 or greater. The cyclic nucleotide binding domain (HMM) has been assigned the PFAM Accession PF00027 (genome.wustl.edu/Pfam/html)(~~http://genome.wustl.edu/Pfam/html~~). An alignment of the cyclic nucleotide binding domain (amino acids 565 to 655 of SEQ ID NO:5) of human 33408 with a consensus amino acid sequence (SEQ ID NO:10) derived from a hidden Markov model is depicted in Figure 4B.

At page 22, line 30 through page 23, line 12, please replace the paragraph with the following text:

As used herein, the term "potassium channel tetramerisation domain" includes an amino acid sequence of about 50 to 200 amino acid residues in length and having a bit score for the alignment of the sequence to the potassium channel tetramerisation domain profile (Pfam HMM) of at least 100. A "potassium channel tetramerisation domain" promotes the assembly of alpha-subunits into functional tetrameric channels. Preferably, a potassium channel tetramerisation domain includes at least about 60 to 150 amino acids, more preferably about 70 to 130 amino acid residues, or about 90 to 110 amino acids and has a bit score for the alignment of the sequence to the potassium channel tetramerisation domain (HMM) of at least 165 or greater. The potassium channel tetramerisation domain (HMM) has been assigned the PFAM Accession Number PF02214 (~~http;~~//genome.wustl.edu/Pfam/.html). An alignment of the potassium channel tetramerisation domain (amino acids 3-101 of SEQ ID NO:8) of human 12189 with a consensus amino acid sequence (SEQ ID NO:11) derived from a hidden Markov model is depicted in Figure 6A.

At page 23, line 19 through page 24, line 2, please replace the paragraph with the following text:

To identify the presence of an "ion transport protein" domain, a "cyclic nucleotide-binding" domain, or a "potassium channel tetramerisation" domain in a 52906, 33408, or 12189 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against the Pfam database of HMMs (e.g., the Pfam database, release 2.1) using the default parameters (~~http://~~www.sanger.ac.uk/Software/Pfam/HMM_search). For example, the hmmsf program, which is

available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (e.g., to 8 bits). A description of the Pfam database can be found in Sonhammer *et al.* (1997) *Proteins* 28(3):405-420 and a detailed description of HMMs can be found, for example, in Gribskov *et al.*(1990) *Meth. Enzymol.* 183:146-159; Gribskov *et al.*(1987) *Proc. Natl. Acad. Sci. USA* 84:4355-4358; Krogh *et al.*(1994) *J. Mol. Biol.* 235:1501-1531; and Stultz *et al.*(1993) *Protein Sci.* 2:305-314, the contents of which are incorporated herein by reference.

At page 33, line 20 through page 34, line 2, please replace the paragraph with the following text:

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at ~~http://~~www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at ~~http://~~www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

At page 34, lines 7-19, please replace the paragraph with the following text:

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to 52906, 33408, or 12189 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to 52906, 33408, or 12189 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See ~~http://~~www.ncbi.nlm.nih.gov.